Process-based expansion and neural differentiation of human pluripotent stem cells for transplantation and disease modeling.

Journal: J Neurosci Res

Publication Year: 2013

Authors: Alexander E Stover, David J Brick, Hubert E Nethercott, Maria G Banuelos, Lei Sun, Diane K O'Dowd, Philip H Schwartz

PubMed link: 23893392

Funding Grants: Immune-Matched Neural Stem Cell Transplantation for Pediatric Neurodegenerative Disease

Public Summary:
Strategies for developing patient-specific, human, induced pluripotent stem cell (iPSC)-based therapies of the brain require an ability to derive large numbers of highly defined neural cells. Here we describe a reliable method for long-term, single-cell passaging of PSCs using a feeder-free, defined culture system that produces confluent, adherent PSCs that can be differentiated into neural stem cells. We demonstrate that this protocol allows for the efficient, large-scale, cGMP-compliant production of transplantable NSCs from all lines tested.

Scientific Abstract:
Robust strategies for developing patient-specific, human, induced pluripotent stem cell (iPSC)-based therapies of the brain require an ability to derive large numbers of highly defined neural cells. Recent progress in iPSC culture techniques includes partial-to-complete elimination of feeder layers, use of defined media, and single-cell passaging. However, these techniques still require embryoid body formation or coculture for differentiation into neural stem cells (NSCs). In addition, none of the published methodologies has employed all of the advances in a single culture system. Here we describe a reliable method for long-term, single-cell passaging of PSCs using a feeder-free, defined culture system that produces confluent, adherent PSCs that can be differentiated into NSCs. To provide a basis for robust quality control, we have devised a system of cellular nomenclature that describes an accurate genotype and phenotype of the cells at specific stages in the process. We demonstrate that this protocol allows for the efficient, large-scale, cGMP-compliant production of transplantable NSCs from all lines tested. We also show that NSCs generated from iPSCs produced with the process described are capable of forming both glia defined by their expression of S100beta and neurons that fire repetitive action potentials. (c) 2013 Wiley Periodicals, Inc.